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12 *Attorneys for Plaintiffs The Regents of the University of Michigan and*
13 *The University of South Florida Board of Trustees*

14 **UNITED STATES DISTRICT COURT**
15 **NORTHERN DISTRICT OF CALIFORNIA**
SAN JOSE DIVISION

16 THE REGENTS OF THE UNIVERSITY OF
MICHIGAN,

17 and

18 THE UNIVERSITY OF SOUTH FLORIDA
BOARD OF TRUSTEES,

19
20 Plaintiffs,

21 v.

22 NOVARTIS PHARMACEUTICALS
23 CORPORATION

24 Defendant.

Case No.

COMPLAINT FOR PATENT INFRINGEMENT

JURY TRIAL DEMANDED

1 This is a civil action for patent infringement of United States Patent No. 10,633,344 (“the
 2 ’344 patent”) under the patent laws of the United States, 35 U.S.C. § 271, *et seq.* Plaintiffs, which
 3 are the corporate entities of two academic institutions, invested in groundbreaking advances in the
 4 fields of chemical engineering and pharmaceutical sciences. As part of Plaintiffs’ investment in
 5 and support of innovative and collaborative research, the named inventors of the ’344 patent—
 6 Drs. Michael Zaworotko, Brian Moulton, and Nair Rodríguez-Hornedo—devoted their individual
 7 expertise in supramolecular technology and pharmaceutical sciences to develop improved
 8 pharmaceutical compounds. Through the inventors’ collaboration, the ’344 patent issued. The
 9 ’344 patent relates to pharmaceutical compositions comprising, among other things,
 10 therapeutically effective amounts of a co-crystal comprising supramolecular synthons with the
 11 claimed elements. Without obtaining a license or permission to use the inventions claimed in the
 12 ’344 patent, Novartis makes, uses, tests, sells, offers for sale and/or imports its co-crystal drug
 13 Entresto®, which directly infringes, literally and/or under the doctrine equivalents, one or more
 14 claims of the ’344 patent.

15 Accordingly, Plaintiffs The Regents of the University of Michigan and The University of
 16 South Florida Board of Trustees (collectively, “Plaintiffs”) file this Complaint and demand for a
 17 jury trial seeking relief for patent infringement by Novartis Pharmaceuticals Corporation
 18 (“Novartis” or “Defendant”). Plaintiffs state and allege the following:

19 **THE PARTIES**

20 1. Plaintiff The Regents of the University of Michigan is a constitutional corporation
 21 of the State of Michigan, having a principal address at Ruthven Building 2300, 1109 Geddes
 22 Avenue, Ann Arbor, Michigan 48109-1079.

23 2. Plaintiff The University of South Florida Board of Trustees is the public body
 24 corporate of the University of South Florida, an academic institution organized and existing under
 25 the laws of the State of Florida, with its principal place of business located at 4202 E. Fowler
 26 Avenue, Tampa, Florida 33620.
 27
 28

1 which is reflected by its extensive patent portfolio covering a wide range of technologies in many
2 disciplines, including chemical engineering and pharmaceutical sciences.

3 19. The University of South Florida is a major research institution designated as a
4 Preeminent State Research University by the Florida Board of Governors and recognized as a top
5 public research university. In 2019, the University of South Florida was awarded \$525.4 million
6 in research grants, putting it at the forefront of research in medicine, science, engineering, the arts,
7 and more.

9 20. As a result of Plaintiffs' investment in and support of innovative and collaborative
10 research, the named inventors of the '344 patent—Drs. Michael Zaworotko, Brian Moulton, and
11 Nair Rodríguez-Hornedo—devoted their individual expertise in supramolecular technology and
12 pharmaceutical sciences to develop improved pharmaceutical compounds.

13 21. Dr. Michael Zaworotko received his Bachelor's in Science from Imperial College
14 in 1977 and a doctorate degree from the University of Alabama in 1982. Dr. Zaworotko was a
15 professor in the chemistry department at the University of South Florida from 1999 to 2013 during
16 the collaborative work that led to the '344 patent. In 2013, Dr. Zaworotko joined the faculty at the
17 University of Limerick, Ireland.

19 22. Dr. Brian Moulton received his doctorate degree in chemistry from the University
20 of South Florida in 2003. During his time at the University of South Florida, Dr. Moulton worked
21 with Dr. Zaworotko, co-authoring several publications related to co-crystal engineering.

23 23. Dr. Nair Rodríguez-Hornedo received a bachelor's degree in pharmacy from the
24 University of Puerto Rico in 1975, and master (1977) and doctorate (1984) degrees in
25 pharmaceutical sciences from the University of Wisconsin-Madison. Dr. Rodríguez-Hornedo was
26 a research scientist in the pharmaceutical industry in 1984-1985, and assistant professor at the
27 University of Arizona in 1985, before joining the faculty at the University of Michigan in 1989.
28

1 Dr. Rodríguez-Hornedo was an associate professor in 1994 and professor in 2016. She was
 2 named professor emerita of pharmaceutical sciences at the University of Michigan in 2022.

3 24. The inventions disclosed in the '344 patent were a result of the collaborative
 4 research performed by Drs. Zaworotko, Moulton, and Rodríguez-Hornedo with the support of the
 5 University of Michigan and the University of South Florida. The '344 patent recognizes the
 6 unmet goal of predictable crystal structure from crystal engineering, *see* **Ex. A** at 1:33-35, and the
 7 patented invention applies the concepts of crystal engineering to design new pharmaceutical
 8 compounds, *id.* at 3:29-34. In particular, the '344 patent relates to “multiple-component solids
 9 having at least one active pharmaceutical ingredient” to achieve crystalline assemblies with
 10 “improved drug solubility, dissolution rate, stability and bioavailability.” *Id.* at 3:12-28.

11
 12
 13 **COUNT I**
Infringement of the '344 Patent Under 35 U.S.C. § 271(a)

14 25. Plaintiffs restate and reallege the preceding paragraphs of this Complaint.

15 26. Novartis has directly infringed, and continues to directly infringe, literally and/or
 16 under the doctrine of equivalents, one or more claims of the '344 patent by making, using, testing,
 17 selling, offering for sale and/or importing into the United States the Accused Products under 35
 18 U.S.C. § 271(a). The Accused Products include the Entresto® tablets at various dose strengths:
 19 low strength (24.3 mg sacubitril, 25.7 mg valsartan); middle strength (48.6 mg sacubitril, 51.4 mg
 20 valsartan); and/or high strength (97.2 mg sacubitril, 102.8 mg valsartan).

21
 22 27. The Accused Products practice all of the elements of at least exemplary claim 10 of
 23 the '344 patent.

24 28. Each dosage strength of Entresto® is a pharmaceutical composition indicated to
 25 reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with
 26 chronic heart failure, and for the treatment of symptomatic heart failure with systemic left
 27
 28

1 ventricular systolic dysfunction in pediatric patients aged one year and older. *See Exhibit B*,
2 Entresto® Drug Label.

3 29. Each dosage strength of Entresto® comprises a pharmaceutically acceptable
4 carrier. For example, Entresto® is a tablet comprising microcrystalline cellulose and other
5 inactive ingredients. *See id.* at 14.

6 30. Each dosage strength of Entresto® comprises a therapeutically effective amount of
7 a co-crystal comprising supramolecular synthons, containing sacubitril-valsartan co-crystals
8 comprising supramolecular synthons. *See Exhibit C* at 1, “LCZ696: A Dual-Action Sodium
9 Supramolecular Complex,” Tetrahedron Letters, 53 (2012) 275-76.

10 31. Each supramolecular synthon is formed from stoichiometric amounts of at least one
11 active pharmaceutical ingredient, for example sacubitril, and one co-former, for example
12 valsartan. **Exhibit B** at 13.

13 32. As one example, an active pharmaceutical ingredient, sacubitril, has a first
14 chemical functionality, a carboxamide, that permits formation of API homosynthons through non-
15 covalent hydrogen bonding when sacubitril is in its pure form. **Exhibit C** at 1.

16 33. As one example, a co-former, valsartan, has a second chemical functionality, a
17 tetrazole, that is complimentary to sacubitril’s first chemical functionality, a carboxamide, via
18 non-covalent hydrogen bonding. *See Exhibit C* at 1.

19 34. As one example, the co-former, valsartan, is a solid at room temperature and
20 atmospheric pressure when valsartan is in its pure form.

21 35. Supramolecular synthons are formed between, as one example, the first chemical
22 functionality of sacubitril, a carboxamide, and the second chemical functionality of valsartan, a
23 tetrazole, via non-covalent hydrogen bonding. *See Exhibit C* at 1.

24 **PRAYER FOR RELIEF**

1 WHEREFORE, Plaintiffs The Regents of the University of Michigan and The University of
2 South Florida Board of Trustees respectfully request that this Court:

- 3 1) Enter judgment that Novartis has infringed one or more claims of the Asserted Patent;
4 2) Award Plaintiffs damages in an amount sufficient to compensate it for Novartis'
5 infringement of one or more claims of the Asserted Patent, together with pre-judgment and
6 post-judgment interest costs, and all other damages permitted under 35 U.S.C. § 284;
7 3) Declare that this be an exceptional case within the meaning of 35 U.S.C. § 285;
8 4) Award Plaintiffs their costs in this action, together with reasonable attorneys' fees and pre-
9 judgment and post-judgment interest;
10 5) Perform an accounting of Novartis' infringing activities through trial and judgment;
11 6) Award Plaintiffs such other and further relief, including other monetary and equitable
12 relief, as this Court deems just and proper.
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17 **DEMAND FOR JURY TRIAL**

18 Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs demand a jury trial on all issues
19 so triable.

20 Dated: August 29, 2022

21 Respectfully Submitted,

22 FISH & RICHARDSON P.C.

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